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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,221	08/19/2003	Hitoshi Nagaoka	1217-031377	6470

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EXAMINER	
MARX, IRENE	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 03/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/644,221	NAGAOKA, HITOSHI	
	Examiner	Art Unit	
	Irene Marx	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-5 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-5 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/519293.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The application should be reviewed for errors.

To facilitate processing of papers at the U.S. Patent and Trademark Office, it is recommended that the Application Serial Number be inserted on every page of claims and/or of amendments filed.

The status of the parent case(s) should be updated.

Claims 1-5 are being considered on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in the recitation of "administering at least one effective dose" even when reading the claim in light of the specification. The method of administration is not set forth with any particularity. There is no indication as whether the mode of administration is oral, intramuscular, intravenous, parenteral, by suppository, etc. In addition, the amount that constitutes "at least one effective dose" to be administered is not defined. There is no clear indication in the written disclosure as to the effectiveness intended by the dose. In addition, the specification indicates that the mycelium extract may be administered to the infected person without dilution or by "appropriately diluting". Yet no indication is found in the as-filed specification as to what amount of the extract, whether diluted or not, it to be administered or how. In addition, the amount of dilution is not set forth with any particularity.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the in vitro treatment of viruses, such as HIV, does not reasonably provide enablement for a method of treating any and all viral diseases *in vivo* , or specifically a method of treating HIV, Hepatitis B infection or liver cancer by administering at least one effective dose of a *Lentinus edodes* extract.. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQd 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

The claims are drawn broadly to a method of treating any and all possible virus diseases, and in particular HIV, Hepatitis B infection and liver cancer using an extract of *Lentinus edodes.*

In view of the enormous diversity of viruses, which includes not only diverse viruses that infect humans, but also diverse viruses that infect simians, dogs, cats, mice, rats, elephants, etc. etc., one of ordinary skill in the art would not reasonably have expected the claim designated extract to effectively treat any viral disease with at least one effective dose of a *Lentinus edodes* extract. To begin with, no "effective dose" of the extract is ever defined or identified in the instant written disclosure. Then, there is no indication as to the mode of administration. Is it oral, intramuscular, intravenous, parenteral, by suppository, etc.? See "list of viruses", wherein most of the viruses are animal viruses.

Moreover, viral infections and HIV infections are notoriously difficult to treat. The effect of the administration of a *Lentinus edodes* extract is not predictable. First, there is the issue of the exact preparation utilized. Not all *Lentinus edodes* extracts are identical, i.e., possess the same or substantially the same active ingredients, even if there is a minimum content of the

unknown active ingredient(s), and they are prepared in the same or substantially the same method, and thus would not work identically. The activities possessed by different fungal preparations would have different effects on different individuals, depending on their age, state of health, weight, sensitivity to allergens. Similarly, *Lentinus edodes* extracts would vary in their purity. In the instant case the size of the openings in the mesh do not appear to be indicated. In addition, Applicant does not disclose the *Lentinus edodes* strains necessary as the source of the extract.

That the extract disclosed inhibits activity of HIV and/or Hepatitis B *in vitro* on MT-4 cells to some extent, cannot be fairly extrapolated to the treatment of any viral diseases in animals or in humans in view of the recognized difficulty in treating viral diseases such as Ebola, Marburg, West Nile virus, rabies, bird flu (H5N1), lyssavirus, HIV and/or Hepatitis B etc. successfully. Regarding liver cancer, there is an accepted association between Hepatitis viruses and some cases of liver cancer, but not all.

Finally, applicants present as a single working embodiment the treatment of MT-4 cells infected with HIV. The data of Table 1, for example, show only inhibition of the HIV virus in MT-4 cells and not in living organisms. No results are shown for hepatitis B. Thus, the in vitro "testing" done on the record fails to correlate with the inhibition of the virus in living animals or humans as claimed with an "at least one effective dose". Regarding the lack of necessary correlation between *in vitro* results and *in vivo* effects regarding the activity of an agent in the setting of HIV-infection see, e.g., Suzuki *et al.* (1989), page 372, paragraph 5. It is mentioned therein that issues such as bioavailability, metabolic features, and toxicities as well as other factors may negate the usefulness of a given agent. The fact that *Lentinus edodes* has been administered orally as a natural nutrient for a long time in Japan, does not ensure that the extract as claimed will be effective in at least one dose to achieve effective concentrations in plasma, for example, to treat viral infections, such as HIV. Another issue to be considered is the degradation and loss of antiviral effects in the complex physiological environment of the human or animal body. Therefore, the results of the instant method of treating appear unpredictable.

While a singular, narrow working embodiment cannot be a sole factor in determining enablement, its limited showing, in light of the unpredictable nature of the art and the direction applicants present, provides additional weight to the lack of enablement in consideration of the

Wands factors as a whole. Thus, one of ordinary skill in the art would not have a reasonable expectation of success in using the claimed invention.

Thus, the scope of the claims is not commensurate with the teachings of enablement of the specification.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amagasse taken with Nagaoka III.

The claims are directed to a method of treating any and all virus disease, and in particular HIV, Hepatitis B infection and liver cancer with at least one effective dose of an extract of *Lentinus edodes.*

Amagasse teach a process of treating Hepatitis B infection using an extract of *Lentinus edodes* cultured on bagasse and defatted rice bran. See, e.g., page 317. To the extent that Hepatitis viruses are associated with liver cancer, one of ordinary skill in the art would have reasonably expected the extract to be suitable for the treatment of liver cancer also.

The reference differs from the claimed invention in that exact process of producing the extract is not disclosed. However, Nagaoka III teaches a method of making an extract of *Lentinus edodes,* which is substantially similar to the recited process, and the product of which would reasonably be expected to be substantially similar to the product used in the instant method of treatment, claims in terms of product-by-process.. See, e.g., Abstract.

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the

same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) (Claim was directed to a Novolac color developer. The process of making the developer was allowed. The difference between the inventive process and the prior art was the addition of metal oxide and carboxylic acid as separate ingredients instead of adding the more expensive pre-reacted metal carboxylate. The product-by-process claim was rejected because the end product, in both the prior art and the allowed process, ends up containing metal carboxylate. The fact that the metal carboxylate is not directly added, but is instead produced in-situ does not change the end product.).

Furthermore, the composition to be used in the claimed method of treatment is claimed as a product-by-process. Since the U.S. Patent and Trademark Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make comparisons therewith, a lesser burden of proof is required to make out a case of prima facie anticipation/obviousness for product-by-process claims because of their peculiar nature than when a product is claimed in the conventional manner. MPEP 2113. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433.

Accordingly, one of ordinary skill in the art would have had a reasonable expectation of success in treating viral diseases such as Hepatitis B and/or diseases associated with Hepatitis B viruses, such as liver cancer, using an extract of *Lentinus edodes* as suggested by the teachings of over Amagasse and Nagaoka III.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the process of over Amagasse, if necessary, by using

a *Lentinus edodes* extract as prepared by Nagaoka III for the expected benefit of treating various viral diseases including Hepatitis B and liver cancer in humans and animals.

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Irene Marx whose telephone number is (571) 272-0919. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 .

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Irene Marx
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Art Unit 1651